

## Vertical sleeve gastrectomy activates GPBAR-1/TGR5 to sustain weight loss, improve fatty liver, and remit insulin resistance in mice.

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### Public Summary:

UNLABELLED: Vertical sleeve gastrectomy (VSG) is one of the most commonly performed clinical bariatric surgeries used for the remission of obesity and diabetes. However, the precise molecular mechanism by which VSG exerts its beneficial effects remains elusive. We report that the membrane-bound G protein-coupled bile acid receptor, GPBAR-1 (also known as TGR5), is required to mediate the effects of anti-obesity, anti-hyperglycemia, and improvements of fatty liver of VSG in mice. In the absence of TGR5, the beneficial metabolic effects of VSG in mice are lost. Moreover, we found that the expression of TGR5 increased significantly after VSG, and VSG alters both BA levels and composition in mice, resulting in enhancement of TGR5 signaling in the ileum and brown adipose tissues, concomitant with improved glucose control and increased energy expenditure. CONCLUSION: Our study elucidates a novel underlying mechanism by which VSG achieves its postoperative therapeutic effects through enhanced TGR5 signaling. (Hepatology 2016;64:760-773).

### Scientific Abstract:

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